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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/870,729	05/30/2001	Anthony P. Shuber	EXT-010CN	9406

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EXAMINER
TUNG, JOYCE

ART UNIT	PAPER NUMBER
1637	14

DATE MAILED: 07/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.	Applicant(s)
09/870,729	Shuber
Examiner	**Art Unit**
Joyce Tung	1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED *Mar 3, 2003* FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

a) ☒ The period for reply expires *6* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see NOTE below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☐ Applicant's reply has overcome the following rejection(s):

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
Please see the attached.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____

Claim(s) objected to: _____

Claim(s) rejected: *16-37*

Claim(s) withdrawn from consideration: _____

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ .

10. ☐ Other:

The amendment filed 3/3/2003 has been entered. Following the entry of the amendment, claims 16-37 are pending.

1. The rejection of claims 28-37 in section (b) under 35 USC §112, second paragraph is withdrawn.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 16, 18-19, 21-23, 25, 28-29, 31-34 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Shuldiner et al. (WO 91/15601).

Shuldiner et al. disclose a method which can be used to distinguish RNA in the sample from contaminating DNA (See pg. 6, lines 23-27). The method applies a first oligonucleotide primer designated d_{20}-t_{21} which comprises the 3' end, a nucleotide sequence complementary to the 3' end of the RNA and the 5' end, a unique random nucleotide sequence or tag which does not hybridize to the RNA sequence within the sample. The primer is extended (See pg. 7, lines 9-24). In the subsequent steps, primers U_{21} and T_{21} are used in which primer U_{21} comprises the sequence complementary to the single stranded DNA segment produced in step 1 and primer T_{21} comprises the unique nucleotide sequence (See pg. 8, lines 11-28). Primer U_{21} is extended (See pg. 9, clines 1-4) and primer T_{21} is extended in second PCR cycle by hybridizing to the unique 5'

sequence (T_{21}) (See pg. 9, lines 6-7). This distinguishes between DNA generated from the RNA-template and possible contaminating DNA (See pg. 7, lines 27-29). The method of Shuldiner et al. leads to logarithmic expansion of the tagged segment of DNA (See pg. 12, lines 26-27).

The response argues that Shuldiner et al. do not teach or suggest the methods recited in amended claims 16 and 28 for detecting cross-sample contamination in the amplification reactions and the method of Shuldiner et al. do not perform the last step recited in either amended claim 16 or amended claim 28, which is determining whether contamination has taken place. However, the method steps of instant invention are the same as the method steps as discussed in the teachings of Shuldiner et al. above. Although Shuldiner et al. do not verbally disclose or suggest the detection of cross-sample contamination. The method of Shuldiner et al. can be used in the detection of cross-sample contamination since the phrase "contamination" is arbitrary. Any nucleic acid sequence in the DNA sample is claimed "contamination".

The response argues that the amplification reaction of Shuldiner et al. has to be conducted in the same sample. Nevertheless, Shuldiner et al. do disclose that in order to evaluate the ability of the RS-PCR method to eliminate problems of carryover contamination of amplified DNA from previous RS-PCR experiments in which another experiment was conducted in which Xenopus pancreatic RNA was reversed transcribed (See pg. 18, lines 20 to pg. 19, lines 1-4). The teachings of Shuldiner indicate that there are two reactions carried out to evaluate the carryover

contamination. One of the reaction is considered to a control amplification reaction. Thus, based upon the discussion above, the rejection is maintained.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 24, 26-27 and 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuldiner et al. (WO 91/15601) as applied to claims 16, 18-19, 21-23, 25, 28-29, 31-34 and 37 above, and further in view of Mullis et al. (4,965,188) .

The teachings of Shuldiner et al. are set forth in section 3 above and Shuldiner et al. do not disclose the limitations of claims 24, 26-27 and 35-36 that the detection is done with sequence specific nucleic acid probe capture and the samples comprise stool and blood.

Mullis et al. disclose that a process for amplifying any target nucleic acid sequence in a nucleic acid mixture (See the Abstract) and a sequence specific probe capture for detection (See column 5, lines 9-12) and the amplification method of Mullis et al. applies to any sample containing target nucleic acid sequence (See column 42-51).

One of ordinary skill in the art at the time of the instant invention would have been motivate to the method of Shuldiner et al. by using the sequence specific probe as taught Mullis et al. to make the instant invention because Mullis et al. disclose that PCR is used to amplify a desired nucleic acid sequence (See the Abstract) and the detection of the nucleic acid sequence is done with a probe (See column 5, lines 8-12). It would have been prima facie obvious to carry out the method as claimed.

The response argues that Shuldiner et al. do not teach detection of cross-sample contamination as presently claimed. However, as discussed in section 3 above, the teachings of Shuldiner et al. read broadly on the limitations of claims 16, 18-19, 21-23, 25, 28-29, 31-34 and 37. Mullis et al. disclose using specific nucleic acid probe capture for detection. It would have been prima facie obvious to combine the references of Shuldiner et al. and Mullis et al. to carry out the method of detecting contamination by amplicon from a previous amplification reaction. Thus, the rejection is maintained.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 17, 20 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 20 is vague and indefinite because of the language "one primer in said control reaction further comprises an additional sequence 3' to said detection sequence". It is unclear what is meant by language. Does it mean that the primer comprises an additional sequence at 3' end which is specific for a target in said previous amplification reaction. Clarification is required.

The response argues that the "additional sequence" is closer to the 3' end of the primer than "said detection sequence" is and the "additional sequence" is at the 3' end of the primer. It is the case. The phrase "additional sequence" is redundant. Thus, the amendment is required.

b. Claims 17 and 30 are vague and indefinite because it is still unclear what is meant by the language "at least one primer in said control reaction is not complementary to any contiguous nucleic acid sequence in said template".

The response argues that no primer recited in claims 17 or 30 is complementary to any continuous stretch of nucleic acid sequence in a target template, say two nucleotides here and three nucleotides there, may together be complementary to part or all of the primer sequence. Based upon the argument, the primers are complementary to nucleic acid in said template. It appears that the language "at least one primer in said control reaction is not complementary to

any contiguous nucleic acid sequence in said template" is conflicting to what the invention is. Thus, the amendment is required.

Therefore, the rejection is maintained.

8. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

J.T

July 25, 2003

JEFFREY SIEW
PRIMARY EXAMINER
7/25/03